08-12-02

1634

#22 (Assist 1)

Attorney's Docket No. 35800/204489 (5718-28A)

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re:	Robison *et al.*	Confirmation No.	9505
Appl. No.:	09/668,266	Group Art Unit:	1634
Filed:	September 22, 2000	Examiner:	B. Sisson
For:	22025, A NOVEL HUMAN CYCLIC NUCLEOTIDE PHOSPHODIESTERASE		

August 9, 2002

Box Non-Fee Amendment
Commissioner for Patents
Washington, DC 20231

AMENDMENT AND REMARKS UNDER 37 C.F.R. § 1.111

Sir:

In response to the Office Action of May 9, 2002, Applicant respectfully requests reexamination and reconsideration of the above-identified application in view of the following amendments and remarks.

Please amend the above-identified application as follows:

In The Claims:

Please amend claim 53 to read as follows:

53. (Amended) A polypeptide comprising an amino acid sequence selected from the group consisting of:

a) a fragment of the amino acid sequence set forth in SEQ ID NO:1, wherein the fragment has phosphodiesterase activity and consists of at least 50 contiguous amino acids of the amino acid sequence set forth in SEQ ID NO:1;

b) a fragment of the amino acid sequence set forth in SEQ ID NO:3, wherein the fragment has phosphodiesterase activity and consists of at least 50 contiguous amino acids of the amino acid sequence set forth in SEQ ID NO:3; and

c) a fragment of the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Patent Deposit Number PTA-1644, wherein said fragment has phosphodiesterase activity and consists of at least 50 contiguous amino acids of the amino acid

D1

sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Patent Deposit Number PTA-1644.

[Please add the following new claims 57-60:]

57. (New) An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

D2

a) the amino acid sequence of a sequence variant of the amino acid sequence set forth in SEQ ID NO:1, wherein the sequence variant has phosphodiesterase activity and has at least 80% sequence identity with the amino acid sequence set forth in SEQ ID NO:1;

b) the amino acid sequence of a sequence variant of the amino acid sequence set forth in SEQ ID NO:3, wherein the sequence variant has phosphodiesterase activity and has at least 80% sequence identity with the amino acid sequence set forth in SEQ ID NO:3; and

c) the amino acid sequence of a sequence variant of the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Patent Deposit Number PTA-1644, wherein said sequence variant has phosphodiesterase activity and has at least 80% sequence identity with the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Patent Deposit Number PTA-1644.

58. (New) The polypeptide of claim 57, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of:

a) the amino acid sequence of a sequence variant of the amino acid sequence set forth in SEQ ID NO:1, wherein the sequence variant has phosphodiesterase activity and has at least 90% sequence identity with the amino acid sequence set forth in SEQ ID NO:1;

b) the amino acid sequence of a sequence variant of the amino acid sequence set forth in SEQ ID NO:3, wherein the sequence variant has phosphodiesterase activity and has at least 90% sequence identity with the amino acid sequence set forth in SEQ ID NO:3; and

c) the amino acid sequence of a sequence variant of the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Patent Deposit Number

PTA-1644, wherein said sequence variant has phosphodiesterase activity and has at least 90% sequence identity with the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Patent Deposit Number PTA-1644.

D2 Cont.

59. (New) The polypeptide of claim 58, wherein said polypeptide comprises the amino acid sequence of a sequence variant of the amino acid sequence set forth in SEQ ID NO:1, wherein the sequence variant has phosphodiesterase activity and has at least 90% sequence identity with the amino acid sequence set forth in SEQ ID NO:1.

60. (New) The polypeptide of claim 58, wherein said polypeptide comprises the amino acid sequence of a sequence variant of the amino acid sequence set forth in SEQ ID NO:3, wherein the sequence variant has phosphodiesterase activity and has at least 90% sequence identity with the amino acid sequence set forth in SEQ ID NO:3.

REMARKS

Status of the Claims

Claims 19, 21, 29, 30, 32-35, and 44-60 are now pending in the application. Claim 53 has been amended as described elsewhere herein. Claims 57-60 have been added. Support for the new claims may be found in the first full paragraph on page 14 of the specification. No new matter has been added by amendment. Reexamination and reconsideration of the claims are respectfully requested.

The Rejections Under 35 U.S.C. 112, First Paragraph Should be Withdrawn

Claims 19, 21, 29, 30, 32-35, and 44-56 have been elected under 35 U.S.C. § 112, first paragraph, on the grounds that they contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The rejection of these claims is respectfully traversed for the reasons described below.

Claims 19, 21, and 29, along with their respective dependent claims have been rejected under 35 U.S.C. § 112, first paragraph on the grounds that the claims recite deposited sequences, and such deposits do not satisfy the written description requirement. However, subsequent to the issuance of the Official Action, the Federal Circuit held that "reference in the specification to a depository, which makes its contents accessible to the public when it is not otherwise available in written form, constitutes an adequate description of the deposited material sufficient to comply with the written description requirement of § 112, ¶ 1. *Enzo Biochem, Inc. v. Gen-Probe Incorporated*, No. 01-1230, 2002 WL 1540813 (Fed. Cir. July 15, 2002). Accordingly, the deposited sequences recited in claims 19, 21, 29, 32-35, and 44-56 meet the requirements for written description under § 112, first paragraph.

Claim 21 has been rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the claimed subject matter is not adequately described. The Examiner states, "[t]o describe the polypeptide in terms of it being comprised of 'heterologous sequences,' when the very underlying amino acid sequence is less than clearly defined, does not add to the clarity, but detracts therefrom." May 9, 2002 Office Action, page . Thus, the rejection appears to be based on the argument that (1) the polypeptide recited in claim 19, from which claim 21 depends, is not adequately described, and (2) the heterologous amino acid sequences recited in claim 21 are not adequately described.

In view of the Federal Circuit's holding in *Enzo* as described above, the polypeptide encoded by the deposited sequence recited in claim 19 meets the requirements for written description, thereby obviating this ground of rejection. Furthermore, in reciting the limitation that the claimed polypeptide comprises the amino acid sequence set forth in SEQ ID NO:1, the amino acid sequence set forth in SEQ ID NO:3, or the amino acid sequence encoded by the cDNA insert contained in ATCC Patent Deposit No. PTA-1644, claim 21 provides the structural features that are characteristic the claimed genus of fusion polypeptides. Accordingly, the written description of the subject matter of claim 21 meets the requirement set forth by the Federal Circuit in *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997), where the court held that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, or chemical name' of the claimed subject matter sufficient to distinguish it from other materials." 119 F.3d at 1568, citing Fiers v. Revel 984 F.2d 1164 (Fed. Cir. 1993).

In addition, the specification discloses several species of fusion polypeptides falling within the scope of the claim. Examples of heterologous amino acid sequences that are encompassed by the claimed fusion polypeptides include GST sequences, beta-galactosidase sequences, poly-His sequences, immunoglobulin sequences, and heterologous signal sequences. *See*, last full paragraph of page 20, *et seq.*, of the specification. Accordingly, the genus of fusion polypeptides recited in claim 21 meets the requirements for a written description of the invention.

Applicant notes that claim 19 and its dependent claims are factually analogous to the hypothetical example presented as Example 8 in the "Revised Interim Written Description Guidelines Training Materials" available at www.uspto.gov/web/menu/written.pdf, and in view of this example these claims meet the requirements for written description. Example 8 of the Training Materials is directed to a claim reciting an isolated and purified nucleic acid comprising SEQ ID NO:2. The conclusion in the Training Materials is that the subject matter of this claim is sufficiently described under § 112, first paragraph, because:

> One of skill in the art can readily envisage nucleic acid sequences which include SEQ ID NO:2 because e.g. SEQ ID NO:2 can be readily embedded in known vectors. Although there may be substantial variability among the species of DNAs encompassed within the scope of the claim because SEQ ID NO:2 may be combined with sequences known in the art, e.g. expression vectors, the necessary common attribute is the ORF (SEQ ID NO:2).
>
> Weighing all factors including (1) that the full length ORF (SEQ ID NO:2) is disclosed and (2) that any substantial variability within the genus arises due to addition of elements that are not part of the inventor's particular contribution, taken in view of the level of knowledge and skill in the art, one skilled in the art would recognized from the disclosure that the applicant was in possession of the genus of DNAs that comprise SEQ ID NO:2.

Revised Interim Written Description Guidelines Training Materials, www.uspto.gov/web/menu/written.pdf. This analysis is supported by the holding of the Federal Circuit in *Hybritech v. Monoclonal Antibodies*, 231 USPQ 81 (Fed. Cir. 1986), where the court stated that what is conventional or well known in the art need not be disclosed in detail. 231 USPQ at 94.

Similarly, in the present application, the Applicants have disclosed the amino acid sequences set forth in SEQ ID NO:1 and SEQ ID NO:3, and have described the public availability of the plasmid deposited with the ATCC as Patent Deposit No. PTA-1644. In addition, the variability present within the genus of polypeptides recited in claims 19 and 21 results from the addition of elements that are not part of the Applicants' particular invention. Accordingly, following the analysis of Example 8, one skilled in the art would

recognize from the disclosure that the Applicants were in possession of the claimed genus of polypeptides that comprise SEQ ID NO:1, SEQ ID NO:3, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Patent Deposit No. PTA-1644.

Claim 29 has been rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the applicant has failed to provide an adequate written description of the claimed polypeptide. The Examiner states that the description of a polypeptide in terms of the structure of the nucleotide sequence that encodes it does not satisfy the requirement for a written description of the claimed invention because, "[e]ven to define a nucleic acid in terms of its ability to encode a polypeptide is not an adequate written description of the nucleic acid as such is to define the nucleic acid in terms of how it is to function, not in terms of what it is." May 9, 2002 Office Action, page 3. Applicant agrees that when a nucleotide sequence of unknown structure is described as encoding a polypeptide of unknown structure, this description constitutes a functional characteristic of the nucleotide sequence. However, this fact pattern does not represent the written description provided for the claimed invention in the present case..

Claim 29 recites a polypeptide comprising an amino acid sequence encoded by a nucleotide sequence having a defined structure, *i.e.*, the claim specifically recites that the nucleotide sequence encoding the amino acid sequence has at least 80% sequence identity with the nucleotide sequence set forth in SEQ ID NO:2 or the nucleotide sequence set forth in SEQ ID NO:4. Because the nucleotide sequences recited in the claim encode the amino acid sequence, the limitations on the structure of the encoding nucleotide sequence necessarily place corresponding limitations on the structure of the amino acid sequences encoded by the nucleotide sequence. Thus, contrary to the statement in the office action, the structural features recited for the encoding nucleotide sequences provide a structural description of the encoded amino acid sequence.

In rejecting claim 29 for lack of written description under 35 U.S.C. § 112, first paragraph, the Examiner further states that "[a] review of the specification finds but two

polypeptide sequences having been adequately described: SEQ ID NO:1 and SEQ ID NO:3. A review of the specification fails to find adequate support for possession or description of any other sequence." May 9, 2002 Office Action, Page 4. The Examiner has further rejected claims 44, 45, 55, and 56 on the grounds that "the specification has not been found to provide an adequate written description of what type and number of amino acid residues can be added to the polypeptide of SEQ ID NO:1 or 3, or fragments thereof, and the resultant polypeptide will still be useful." May 9, 2002 Office Action, page 4. Thus, the Examiner appears to be arguing that only those species whose sequences are specifically disclosed in the specification are adequately described under 35 U.S.C. § 112, first paragraph. However, the requirement set forth in the office action is not supported by the "Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, 'Written Description' Requirement" (66 Fed. Reg. 1099 (2001)) and the supporting case law.

The "Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, 'Written Description' Requirement" state that genus may be described by "sufficient description of a representative number of species . . . or by disclosure of relevant, identifying characteristics, *i.e.* structure or other physical and/or chemical properties." *Id.* at 1106. This requirement is in accordance with *Regents of the University of California v. Eli Lilly & Co*, 119 F.3d 1559 (Fed. Cir. 1997), where the court held that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, or chemical name' of the claimed subject matter sufficient to distinguish it from other materials." 119 F.3d at 1568, citing Eiers v. Revel 984 F.2d 1164 (Fed. Cir. 1993).

Applicant submits that the written description provided for the sequences recited in claims 29, 30, 32-35, and 44-56 meets this requirement. These claims recite the identifying structural characteristics that define each genus of nucleotide sequences. Claims 29-35 and 48-52 recite a polypeptide encoded by a nucleotide sequence that has at least a designated level of sequence identity with SEQ ID NO:2 or SEQ ID NO:4, or that hybridizes under defined conditions to the cDNA insert contained in ATCC Patent Deposit No. PTA-1644. Claims 44, 45, and 46 recited polypeptides comprising the amino acid sequence set forth in SEQ ID NO:1 or

SEQ ID NO:3, or the amino acid sequence encoded by the cDNA insert contained in ATCC Patent Deposit No. PTA-1644. Claims 53-56 recite the amino acid sequence of a fragment of the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:3, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Patent Deposit Number PTA-1644, wherein said fragment consists of at least 50 contiguous amino acids of the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:3 or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Patent Deposit Number PTA-1644. These structural limitations are sufficient to distinguish the claimed polypeptides from other materials and thus sufficiently define the claimed genus.

Furthermore, in *Lilly*, the court held that "[a] description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." 119 F.3d at 1569. The recitation of the structural features of amino acid sequences encoded by nucleotide sequences that have sequence identity with SEQ ID NO:2 or SEQ ID NO:4 or hybridize to the cDNA insert of the plasmid deposited with ATCC as Patent Deposit Number PTA-1644 under specified conditions, amino acid sequences that are disclosed in the Sequence Listing or encoded by deposited coding sequences, or amino acid sequences of fragments of SEQ ID NO:1 or SEQ ID NO:3 or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Patent Deposit Number PTA-1644, where the fragments have a given minimum length, is sufficient to satisfy this requirement.

Applicant has further provided the functional characteristics that distinguish the genus of sequences. Specifically, claims 29, 30, 32-34, and 47-56 recite that the members of the claimed genera of variants or fragments have phosphodieseterase activity. Accordingly, both the structural properties and the functional properties that characterize the claimed genus are specifically recited in the claims.

The Examiner has continued to argue that claims 32, 33, and 47-52 do not recite a limitation to any particular functional activity. See, page 6 of the Office Action mailed May 9,

2002. However, claims 32, 33, and 47-52 all depend from claim 29, and claim 29 specifically recites "[a] polypeptide having phosphodiesterase activity." The Code of Federal Regulations provides that "[o]ne or more claims may be presented in dependent form, referring back to and *further limiting* another claim or claims in the same application." 37 C.F.R. § 1.75 (2001), emphasis added. Accordingly, dependent claims 32, 33, and 47-52 necessarily contain the functional limitation recited in independent claim 29.

Claims 19, 21, and 44-46 recite amino acid sequences that are provided in the sequence listing and amino acid sequences that are encoded by a deposited cDNA. The Examiner correctly observes that claims 19, 21, and 44-46 do not recite a functional limitation. Applicants note that the complete structure of the recited amino acid sequences is provided in the specification or can be determined based on the deposited cDNA. Applicants know of no authority, binding or otherwise, which states that Applicants who claim a polypeptide having a sequence disclosed in the specification must also provide the functional characteristics of the claimed polypeptide. When the structure of the amino acid sequence is disclosed, and this structure is sufficient to distinguish the claimed invention from other materials, no further information is required to sufficiently describe the invention.

As described in Applicants' Amendment mailed February 20, 2002, the present claims are analogous to those presented in Example 14 of the "Revised Interim Written Description Guidelines Training Materials" available at www.uspto.gov/web/menu/written.pdf. Example 14 is directed to a generic claim: a protein having at least 95% sequence identity to the sequence of SEQ ID NO:3, wherein the sequence catalyzes the reaction A → B. The conclusion in the Training Materials is that the generic claim of Example 14 is sufficiently described under § 112, first paragraph, because 1) "the single sequence disclosed in SEQ ID NO:3 is representative of the genus" and 2) the claim recites a limitation requiring the compound to catalyze the reaction from A → B, and therefore one of skill in art would recognize that the Applicant was in possession of the necessary common attributes possessed by the members of the genus.

Following the analysis of Example 14, Applicant submits that claims 19, 21, 29, 30, 32-35, and 44-46 satisfy the written description requirements of § 112, first paragraph. Specifically,

these claims encompass amino acid sequences having a disclosed sequence, sequence variants encoded by nucleotide sequences having a specified level of sequence identity with SEQ ID NO:2 or SEQ ID NO:4, or by nucleotide sequences hybridizing to the cDNA insert of the plasmid deposited with ATCC as Patent Deposit No. PTA-1644 and fragments comprising a subsequence of SEQ ID NO:1, SEQ ID NO:3, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Patent Deposit Number PTA-1644, wherein the claimed sequences encode a polypeptide having a specified activity. As in Example 14, the specification discloses the nucleic acid sequence of SEQ ID NO:2 and SEQ ID NO:4, as well as the encoded polypeptides SEQ ID NO:1 and SEQ ID NO:3, and claims 29, 30, 32, 33, and 47-56 recite a limitation requiring the compound to have a specific function (*i.e.* phosphodiesterase activity). Accordingly, claims 19, 21, 29, 30, 32-35, and 44-46 provide the relevant, identifying characteristics that describe the claimed genus, and one of skill in the art would recognize that the inventors were in possession of the claimed invention. Therefore, the requirement for a written description of the claimed invention under 35 U.S.C. § 112, first paragraph is met.

In responding to the arguments presented by the Applicants in support of the written description of the claims, the Examiner states, "it is asserted that the claimed invention is adequately described as the claims have been defined in part by the activity of the isolated polypeptide." However, this is not an accurate characterization of Applicants' arguments of record. In the Amendment mailed February 20, 2002, Applicants stated:

> In the present case, the recited sequences in claims 88-91 have been described by both their structural properties and functional characteristics, thereby meeting the standards set forth in the guidelines. The present claims are comparable to the claim presented in Example 14 of the "Synopsis of Application of Written Description Guidelines" cited in the written description guidelines (66 Fed. Reg. 1101), in which the claimed protein is described by its sequence identity with a second protein and by its function. In the analysis of this example in the Synopsis, it is concluded that the claimed polypeptide is adequately described. Similarly, in the present case the criteria for written description have been met and the rejection should be withdrawn.

February 20, 2002 Amendment, page 7. Accordingly, contrary to the statement in the Office Action, Applicants have not argued that the present claims meet the written description requirement because "they have been defined in part by the activity of the isolated polypeptide."

Claims 19, 21, 44-46, 53, and 54 have been rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the specification fails to provide sufficient enablement to allow one of skill in the art to make and use the polypeptides recited in these claims. The Examiner argues that these claims do not specifically recite that the claimed polypeptides have phosphodiesterase activity and that "the specification has not been found to teach a reproducible method of using an inactive form of the polypeptide." Thus, the Examiner's rejection appears to be based on the premise that the Applicants have not demonstrated that polypeptides having the amino acid sequences set forth in SEQ ID NO:1 and SEQ ID NO:3 function as phosphodiesterases. In fact, Applicant has demonstrated the function of the 22025 receptor using art-accepted methods, and therefore one of skill in the art would know how to use the polypeptides recited in claims 19, 21, 44-46, 53, and 54.

The 22025 polypeptides of SEQ ID NO:1 and SEQ ID NO:3 have been compared to the Pfam database of protein families and been shown to share a high score when compared with the consensus domain for the 3'5'-cyclic nucleotide phosphodiesterases (PFAM Accession No. PF00233; see figures 2 and 7). The Pfam database provides a curated collection of well-characterized protein family domains with high quality alignments. Functional domains of novel proteins may be identified by comparison with the Pfam protein family domain alignments. It is well known in the art that regions of sequence homology with known functional domains may be used to determine protein function. The proteins included in the Pfam seed alignment for the cyclic nucleotide phosphodiesterase consensus sequence include numerous GPCRs that have been well-characterized biochemically. Accordingly, the presence of a Pfam cyclic nucleotide phosphodiesterase domain in the 22025 sequence indicates that 22025 functions a cyclic nucleotide phosphodiesterase.

Alternatively, if the Examiner's rejection of claims 19, 21, 44-46, 53, and 54 under 35 U.S.C. § 112, first paragraph, for lack of enablement is based on the grounds that a polypeptide having the amino acid set forth in SEQ ID NO:1, SEQ ID NO:3, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Patent Deposit No. PTA-1644 encompasses polypeptides having additional amino acid sequences (such as, for example, GST sequences, beta galactosidase sequences, or poly-His sequences) that might interfere with the phosphodiesterase activity of the claimed polypeptides, Applicants note that the specification does provide guidance regarding the use of the claimed polypeptides that do not rely on the phosphodiesterase activity of these polypeptides. For example, the specification teaches the use of 22025 polypeptides as immunogens useful for producing antibodies specific for the phosphodiesterase. *See*, pages 35-36 of the specification. The specification also provides guidance for the use of polypeptides comprising the 22025 amino acid sequence and an additional "tag sequence" in purification of 22025 polypeptides. *See*, lines 1-4 of page 21 of the specification. Accordingly, given the guidance provided in the specification, one of skill in the art could make and use the polypeptides recited in claims 19, 21, 44-46, 53, and 54.

Claims 19, 21, 29, 32-35, and 44-56 have been rejected on the grounds that the claimed invention lacks utility and therefore one of skill in the art would not no use to use it. Applicants present arguments below demonstrating that the invention of claims 19, 21, 29, 32-35, and 44-56 does have patentable utility and therefore one of skill would know how to use it. Accordingly, the rejection is respectfully traversed.

In view of the above arguments, all grounds for rejection under 35 U.S.C. § 112, first paragraph, have been overcome. Reconsideration and withdrawal of the rejections are therefore respectfully requested.

The Rejections Under 35 U.S.C. § 112, Second Paragraph, Should be Withdrawn

Claims 19, 21, 44-46, 53, and 54 have been rejected under 35 U.S.C. § 112, second paragraph, on the grounds that they fail to set forth the subject matter which the Applicants regards as their invention. The Examiner argues that because these claims do not recite a functional limitation, they do not correspond in scope with that which the Applicants regard as the invention. As support for this argument, the Examiner refers the Applicants to the Amendment mailed November 20, 2001, in which the Applicants stated that "the claimed genus in the present application is defined in the specification by the functional properties (*i.e.* phosphodiesterase activity) and the structural properties." The Examiner argues that this statement indicates that the invention is different from what is defined in the claims because claims 19, 21, 44-46, 53, and 54 do not recite that the claimed polypeptides have phosphodiesterase activity.

Applicants note that the arguments cited by the Examiner were directed to the Examiner's rejection of claims 26, 27, 29, 30, 32-35, 37-39, 41, and 42 for lack of written description. In the Office Action mailed August 21, 2001, claims 19, 21, 44-46, 53, and 54 were not rejected for insufficient written description. Accordingly, the cited statement applies only to the rejected claims, and one of skill in the art would be able to determine the metes and bounds of the claims as written.

Claims 29, 30, 34, 35, 53, and 54 have been rejected under 35 U.S.C. § 112, second paragraph, on the grounds that these claims are indefinite because they recite heterologous amino acid sequences. In fact, the specification describes the use of heterologous amino acid sequences and gives examples of sequences that are encompassed by the claimed fusion polypeptides, including GST sequences, beta-galactosidase sequences, poly-His sequences, immunoglobulin sequences, and heterologous signal sequences. *See*, last full paragraph of page 20, *et seq.*, of the specification. Additionally, heterologous amino acid sequences that may be fused to an amino acid sequence of interest are well know to those of skill in the art. Accordingly, claims 29, 30, 34, 35, 53, and 54 meet the requirements for definiteness as stated by the Board of Patent

Appeals and Interferences, because one of ordinary skill in the art, when reading the claims in light of the supporting specification, would be able to ascertain with a reasonable degree of precision and particularity the particular area set out and circumscribed by the claims. *Ex parte* Wu, 10 USPQ 2d 2031, 2033 (B.P.A.I. 1989).

In view of the above arguments, all grounds for rejection under 35 U.S.C. § 112, second paragraph, have been overcome. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

The Rejection Under 35 U.S.C. § 101 Should be Withdrawn

Claims 19, 21, 44-47, and 53-54 have been rejected under 35 U.S.C. § 101 on the grounds that the claimed invention lacks patentable utility. The rejection is respectfully traversed for the reasons described below.

The Examiner argues that claims 19, 21, 44-47, and 53-54 encompass polypeptides that lack phosphodiesterase activity, and that polypeptides lacking phosphodiesterase activity are considered to lack. It is unclear to the Applicants whether the Examiner is arguing that a prima facie case of no utility has been met because the Examiner does not accept that the polypeptides of SEQ ID NO:1, SEQ ID NO:3, or the polypeptide encoded by the cDNA insert deposited with the ATCC at Patent Deposit No. PTA-1644 have phosphodieseterase or activity, or because the claims as written encompass polypeptides having amino acid sequences heterologous to SEQ ID NO:1, SEQ ID NO:3, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC as Patent Deposit No. PTA-1644, and that these heterologous sequences might interfere with the phosphodiesterase activity of SEQ ID NO:1, SEQ ID NO:3, or the amino acid sequence encoded by the cDNA insert deposited with the ATCC as Patent Deposit No. PTA-1644. Therefore, both lines of argument are addressed below.

The "Examination Guidelines for the Utility Requirement" (MPEP § 2107) set forth the elements required to establish a *prima facie* case of no utility as follows:

> Where the asserted utility is not specific or substantial, a *prima facie* showing must establish that it is more likely than not that a person of ordinary skill in the art would not consider that any utility asserted by the applicant would be specific and substantial. The prima facie showing must contain the following elements:
>
> (i) An explanation that clearly sets forth the reasoning used in concluding that the asserted utility for the claimed invention is not both specific and substantial nor well-established;
>
> (ii) Support for factual findings relied upon in reaching this conclusion; and
>
> (iii) An evaluation of all relevant evidence of record, including utilities taught in the closest prior art.

MPEP § 2107. This is in accordance with *In re Brana*, 34 U.S.P.Q.2d 1437, 1441 (Fed. Cir. 1995), where the Federal Circuit held that, "[o]nly after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the Applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility.")

The Applicants have demonstrated that the 22025 polypeptides of SEQ ID NO:1 and SEQ ID NO:3, and the polypeptide encoded by the cDNA insert of the plasmid deposited with ATCC as Patent Deposit No. PTA-1644 function as phosphodiesterases using methods that are well-accepted in the art. These polypeptides have been compared to the Pfam database of protein families and been shown to share a high score when compared with the consensus domain for the 3'5'-cyclic nucleotide phosphodiesterases (PFAM Accession No. PF00233; see figures 2 and 7).

The Pfam database provides a curated collection of well-characterized protein family domains with high quality alignments. Functional domains of novel proteins may be identified by comparison with the Pfam protein family domain alignments. It is well known in the art that regions of sequence homology with known functional domains may be used to determine protein function. The proteins included in the Pfam seed alignment for the cyclic nucleotide

phosphodiesterase consensus sequence include numerous GPCRs that have been well-characterized biochemically. Accordingly, the presence of a Pfam cyclic nucleotide phosphodiesterase domain in the 22025 sequence indicates that 22025 functions a cyclic nucleotide phosphodiesterase. Furthermore, the Examiner has presented no evidence to support the argument that the recited amino acid sequences have phosphodiesterase activity. Therefore, the Examiner's burden of establishing a *prima facie* case of no utility has not been met.

Alternatively, if the Examiner's rejection of claims 19, 21, 44-46, 53, and 54 under 35 U.S.C. § 101 for lack of patentable is based on the grounds that a polypeptide having the amino acid set forth in SEQ ID NO:1, SEQ ID NO:3, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Patent Deposit No. PTA-1644 encompasses polypeptides having additional amino acid sequences (such as, for example, GST sequences, beta galactosidase sequences, or poly-His sequences) that might interfere with the phosphodiesterase activity of the claimed polypeptides, Applicants note that the specification asserts utilities for the claimed polypeptides that do not rely on the phosphodiesterase activity of these polypeptides. For example, the specification teaches the use of 22025 polypeptides as immunogens useful for producing antibodies specific for the phosphodiesterase. *See*, pages 35-36 of the specification. The specification describes the use of polypeptides comprising the 22025 amino acid sequence and an additional "tag sequence" in purification of 22025 polypeptides. *See*, lines 1-4 of page 21 of the specification. Accordingly, Applicants have asserted specific and substantial, and credible utilities for both enzymatically active and enzymatically inactive polypeptides encompassed by claims 19, 21, 44-47, and 53-54. Furthermore, the Examiner has presented no evidence or factual findings to demonstrate that the polypeptides of claims 19, 21, 44-46, 53, and 54 lack utility. Accordingly, a *prima facie* case of no utility has not been established.

In view of the above arguments, all grounds for rejection under 35 U.S.C. § 112, second paragraph, have been overcome. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

CONCLUSION

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR §1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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